

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 13751-035WO1	<b>FOR FURTHER ACTION</b>		See item 4 below
International application No. PCT/US2004/011745	International filing date ( <i>day/month/year</i> ) 16 April 2004 (16.04.2004)	Priority date ( <i>day/month/year</i> ) 18 April 2003 (18.04.2003)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant BIOGEN IDEC MA INC.			

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- |   |   |
|---|---|
| <input checked="" type="checkbox"/> Box No. I | Basis of the report   |
| <input type="checkbox"/> Box No. II           | Priority  |
| <input type="checkbox"/> Box No. III          | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| <input type="checkbox"/> Box No. IV           | Lack of unity of invention  |
| <input checked="" type="checkbox"/> Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> Box No. VI           | Certain documents cited   |
| <input type="checkbox"/> Box No. VII          | Certain defects in the international application  |
| <input type="checkbox"/> Box No. VIII         | Certain observations on the international application   |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No. +41 22 740 14 35	Date of issuance of this report 18 April 2006 (18.04.2006)
	Authorized officer  Yoshiko Kuwahara  Telephone No. +41 22 338 90 90

# PATENT COOPERATION TREATY

REC'D 13 MAR 2006

WIPO

EST

From the  
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:  
JACK BRENNAN  
FISH & RICHARDSON P.C.  
45 ROCKEFELLER PLAZA  
SUITE 2800  
NEW YORK, NY 10111

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing  
(day/month/year) **08 MAR 2006**

Applicant's or agent's file reference

13751-034WO1

**FOR FURTHER ACTION**

See paragraph 2 below

International application No.

PCT/US04/11745

International filing date (day/month/year)

16 April 2004 (16.04.2004)

Priority date (day/month/year)

18 April 2003 (18.04.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(8): A61K 38/00 and US Cl.: 514/12

Applicant

BIOGEN IDEC MA INC

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Date of completion of this  
opinion

06 February 2006 (06.02.2006)

Authorized officer

Daniel C. Samet, PhD

Telephone No. 571 272 1600

Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/11745

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:  
☒ the international application in the language in which it was filed  
☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material  
☐ a sequence listing  
☒ table(s) related to the sequence listing
  - b. format of material  
☐ on paper  
☒ in electronic form
  - c. time of filing/furnishing  
☐ contained in the international application as filed.  
☐ filed together with the international application in electronic form.  
☒ furnished subsequently to this Authority for the purposes of search.
3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
PCT/US04/11745

**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Claims <u>7-11, 13-22</u>	YES
	Claims <u>1-6, 12-14, 23, 24</u>	NO
Inventive step (IS)	Claims <u>15, 16</u>	YES
	Claims <u>1-14, 16-24</u>	NO
Industrial applicability (IA)	Claims <u>1-24</u>	YES
	Claims <u>NONE</u>	NO

**2. Citations and explanations:**

The prior art teaches that neublastin, also known as artemin, is a GDNF-related factor that activates RET receptors (Boloh et al, Neuron 21:1291-1302, 1998). Neublastin/artemin is a glycosylated dimer (e.g. US 6593133 B1, column 3, lines 33-44; column 12, lines 29-31). Modification of artemin with polyethylene glycol is taught in WO 02/051433 (page 35, lines 29-31). Use of artemin to treat neuropathic pain is taught in WO 02/051433 (page 62, lines 1-14). Together, these references fully anticipate or render obvious claims 1-14 and 17-24 of the instant application.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/11745

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>																						
IPC(8) : A61K 38/00																						
US CL : 514/12																						
According to International Patent Classification (IPC) or to both national classification and IPC																						
<b>B. FIELDS SEARCHED</b>																						
Minimum documentation searched (classification system followed by classification symbols)																						
U.S. :																						
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched																						
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)																						
Medline, Caplus, Embase, Biosis																						
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>																						
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.																				
X	WO 02/051433 A2 (Shelton et al) 4 July 2002 (04.07.2002), page 35, lines 29-31; SEQ ID NO:1 Page 62, lines 1-14	1-6, 12-14, 23, 24																				
Y		7-11, 17-22																				
Y	US 6284540 (Milbrandt et al.) 4 September 2001 (04.09.2001), columns 14-15, columns 25, lines 45-60; figures 10, 11; SEQ ID NO: 3	1-13, 23																				
Y, E	US 6593133 B1 (Johansen et al) 15 Jul 2003 (15.07.2003); SEQ ID NOS: 2, 4-7, 9, 12; column 12, lines 29-31	1, 2																				
Y	Baloh, et al., 1998. Artemin, a novel member of the GDNF ligand family, supports peripheral and central neurons and signals through the GFR.alpha.3-RET receptor complex. Neuron 21: 1291-1302, Dec.	23																				
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.																						
* Special categories of cited documents: <table border="0"> <tr> <td>"A"</td> <td>document defining the general state of the art which is not considered to be of particular relevance</td> <td>"T"</td> <td>later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</td> </tr> <tr> <td>"E"</td> <td>earlier application or patent published on or after the international filing date</td> <td>"X"</td> <td>document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</td> </tr> <tr> <td>"L"</td> <td>document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</td> <td>"Y"</td> <td>document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</td> </tr> <tr> <td>"O"</td> <td>document referring to an oral disclosure, use, exhibition or other means</td> <td>"&amp;"</td> <td>document member of the same patent family</td> </tr> <tr> <td>"P"</td> <td>document published prior to the international filing date but later than the priority date claimed</td> <td></td> <td></td> </tr> </table>			"A"	document defining the general state of the art which is not considered to be of particular relevance	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	"E"	earlier application or patent published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	"O"	document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family	"P"	document published prior to the international filing date but later than the priority date claimed		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention																			
"E"	earlier application or patent published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone																			
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art																			
"O"	document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family																			
"P"	document published prior to the international filing date but later than the priority date claimed																					
Date of the actual completion of the international search		Date of mailing of the international search report																				
06 February 2006 (06.02.2006)		08 MAR 2006																				
Name and mailing address of the ISA/US		Authorized officer																				
Mail Stop PCT, Attn: ISA/US		Daniel C. Garnett, PhD																				
Commissioner for Patents		Telephone No. 571 272 1600																				
P.O. Box 1450																						
Alexandria, Virginia 22313-1450																						
Facsimile No. (571) 273-3201																						